IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
AUSTIN DIVISION

MAX WELLS,	§	
	§	
PLAINTIFF,	§	
	§	
vs.	§	CAUSE NO. A-06-CA-126-LY
	§	
SMITHKLINE BEECHAM	§	
CORPORATION,	§	
	§	
DEFENDANT.	§	

MOTION TO PRECLUDE PROPOSED EXPERT TESTIMONY PURSUANT TO FEDERAL RULES OF EVIDENCE 702 AND 703 AND FOR SUMMARY JUDGMENT ("*DAUBERT/HAVNER* MOTION")

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PRELIMINARY STATEMENT

Pursuant to Federal Rules of Evidence 702 and 703 and Federal Rule of Civil Procedure 56, Defendant SmithKline Beecham Corporation d/b/a GlaxoSmithKline ("GSK") files this motion ("*Daubert/Havner* Motion") for an order precluding the proposed testimony of Dr. Wells' designated expert witnesses and granting GSK summary judgment on the grounds that (i) the witnesses' opinions as to causation are scientifically unreliable and (ii) the expert witness who has rendered an opinion as to GSK's claimed failure to warn is unqualified to render such an opinion;[1] and in support, respectfully shows as follows:

INTRODUCTION

Dr. Wells claims that he had a "gambling compulsion" (First Amended Complaint of Max Wells ("Complaint"), ¶14)[2] and lost approximately $14 million as the result of his treatment with Requip (ropinirole hydrochloride),[3] a medication manufactured by GSK and approved by the Food and Drug Administration ("FDA") for the treatment of idiopathic Parkinson's disease. Dr. Wells asserts that GSK's failure to provide adequate warnings was the "causative nexus" of his gambling compulsion, *id.*, ¶19, even though there is not a single study in the scientific literature showing a statistically significant association between treatment with Requip and pathological gambling and it is not generally accepted in the scientific community that Requip causes pathological gambling. Indeed, ***Dr. Wells' own experts have conceded that it is not***

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[1] GSK has separately moved for summary judgment on the ground that Dr. Wells lacks evidence of causation. *See Motion for Summary Judgment as to Causation.*

[2] Dr. Wells appears to equate "compulsive gambling" with "pathological gambling," the term his proposed experts use to describe his alleged condition during the period he took Requip. GSK disputes that Dr. Wells met the criteria for a diagnosis of pathological gambling during the period he took Requip or at any other time.

[3] The trade name is Requip, and the generic name is ropinirole hydrochloride.

established that Requip causes pathological gambling, as explained in GSK's *Motion for Summary Judgment as to Causation*, filed herewith and incorporated by reference.

Dr. Wells' theory of liability is that GSK "failed to warn the public or physicians" that "Parkinson's disease patients using Requip could develop an irresistible gambling compulsion as a side effect of taking the drug" (Complaint ¶18). To recover on this theory, Dr. Wells must – in addition to proving that GSK failed to warn about a possible connection between Requip and pathological gambling – prove both general causation and specific causation. "General causation is whether a substance is capable of causing a particular injury or condition in the general population, while specific causation is whether a substance caused a particular individual's injury." *Merrell Dow Pharm., Inc. v. Havner*, 953 S.W.2d 706, 714 (Tex. 1997; *Minnesota Mining & Mfg. Co. v. Atterbury*, 978 S.W.2d 183, 203 (Tex. App—Texarkana 1998 (plaintiff "must prove both general and specific causation. In other words, a plaintiff must prove that the agent he or she alleges caused injury or illness 1) could do so in the general population, and 2) did so to him or her specifically"). Thus, Dr. Wells here must prove: (i) that Requip can cause pathological gambling in Parkinson's disease patients and (ii) that Requip caused his claimed pathological gambling and gambling losses.

Dr. Wells has identified three proposed expert witnesses, Timothy Fong, M.D., a psychiatrist; Ari Kalechstein, Ph.D., a psychologist; and Stephen R. Saklad, Pharm. D., a pharmacist, each of whom has provided an expert report and given deposition testimony. To the extent they purport to address general causation, Dr. Wells' designated experts reference published literature addressing the ***possibility*** that there is a relationship between treatment with dopamine agonists, a class of Parkinson's disease medications that includes Requip, and the development of pathological gambling. As discussed in *GSK's Motion for Summary Judgment*

as to Causation, the concessions by Dr. Wells' experts that the scientific literature does not establish that Requip causes pathological gambling should end the causation inquiry as a matter of law. The purpose of this motion is to show that, even apart from these concessions, the scientific literature would not support a general causation opinion that would be admissible under *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 113 S. Ct. 2786 (1993) and *Havner*, 953 S.W.2d 706. No study shows a statistically significant association between Requip and pathological gambling, and it is not generally accepted that Requip causes pathological gambling. In short, this motion explains why Dr. Wells' experts had to concede that there is no reliable scientific evidence that Requip causes pathological gambling and why Dr. Wells' claims therefore fail as a matter of law.

Independently, Dr. Wells' claims against GSK fail for lack of competent proof of specific causation. In asserting that Dr. Wells' alleged pathological gambling was caused by Requip, Dr. Wells' experts rely on the claimed temporal relationship between Dr. Wells' increased gambling and his treatment with Requip; but they have failed to consider—much less exclude—other plausible causes of Dr. Wells' increased gambling, as well as reasons that may explain why Dr. Wells stopped gambling at the time he stopped taking Requip. As a result, the experts' opinions as to specific causation are scientifically unreliable. Dr. Saklad's opinion should also be precluded for the further reason that, as a pharmacist, he is wholly unqualified to address specific causation and because the sole basis for his case-specific opinions is his review of Dr. Wells' First Amended Complaint. Remarkably, Dr. Saklad has offered a case-specific opinion even though he has not read a single medical record, has not interviewed Dr. Wells, and has not reviewed a single deposition transcript of Dr. Wells, his family members, or his treating physicians.

For any and all of these reasons, any causation testimony by Dr. Wells' experts should be precluded pursuant to Federal Rules of Evidence 702 and 703, and pursuant to the *Daubert* and *Havner* decisions and their progeny; and absent admissible evidence to prove both general and specific causation, GSK should be granted summary judgment dismissing Dr. Wells' First Amended complaint pursuant to Federal Rule of Civil Procedure 56.

One of Dr. Wells' experts, Dr. Saklad, additionally purports to give expert opinions as to the adequacy of the FDA-approved labeling for Requip. Yet, as he has conceded, Dr. Saklad has no experience or training whatsoever with regard to prescription drug labeling and related FDA regulations, and he is accordingly unqualified to offer any opinions regarding GSK's alleged failure to warn. Because expert testimony is required to support Dr. Wells' failure to warn claim, GSK should be granted summary judgment dismissing Dr. Wells' First Amended Complaint on this ground as well.

FACTS

A. Background[4]

The plaintiff, Dr. Wells, is a board-certified clinical pathologist licensed to practice medicine in the State of Texas, who was diagnosed with idiopathic Parkinson's disease in April 2000. Deposition of Max Wells at Volume 1, 30:9-13; 34:11-15; Vol. 2, 16:2-24 ("Wells Depo.") (Exhibit A).[5] Dr. Wells alleges that he began taking Requip to treat his Parkinson's

[4] This "Background" section is identical to the one contained in GSK's *Motion for Summary Judgment as to Causation*. *See* note 1, *supra*. It is reprinted in both motions for the Court's convenience.

[5] The exhibits supporting this motion and GSK's contemporaneously filed *Motion for Summary Judgment as to Causation* and *Motion for Summary Judgment on Preemption* are contained in a separately filed *Documentary Evidence Notebook in Support of Motions for Summary Judgment and Daubert/Havner Motion*. Subsequent references to the five-volume Wells' Depo. will be abbreviated to list the Volume and page and line numbers, *e.g.*: "Wells Depo. Vol. 1, 4:25-5:1."

disease in the fall of 2004. Complaint ¶ 13; *see also* Wells Depo. at Vol. 4, 80:23-81:3. Parkinson's disease is a progressive, neurodegenerative disorder that occurs when certain dopamine-producing brain cells begin to die, resulting in a loss of coordinated movement and initiated movement, among other symptoms. *See* Deposition of Sara A. Westgate, M.D., Ph.D at 270:4-20; 273:8-274:5 ("Westgate Depo.") (Exhibit B). Requip is a dopamine agonist, which is "essentially a dopamine mimicker" and acts like dopamine in the brain. *Id.* at 275:3-13. It has been effective in a number of Parkinson's disease patients, including Dr. Wells, in alleviating the symptoms of Parkinson's disease. *Id.* at 259:10-13; 261:11-262:12.

At the time Dr. Wells began taking Requip, the FDA-approved labeling did not mention gambling, although it was revised during the course of his treatment to disclose a possible association between the two. *See* GSK's *Motion for Summary Judgment as to Preemption*, filed contemporaneously and incorporated by reference. Although Dr. Wells had reviewed an article suggesting a possible association between certain Parkinson's disease drugs and pathological gambling and had discussions with his neurologist that his increased gambling might be related to the drugs he was taking—*see* Westgate Depo. at 163:16-164:1; 165:19-166:9; 175:4-17; 223:16-225:4; *see also* Wells Depo. Vol. 3, 81:9-16; Vol. 4, 51:6-20 and Exhibit 26—Dr. Wells claims here that GSK's warnings were at all times inadequate to inform him of the risk. Complaint ¶ 18. Dr. Wells asserts that GSK's "failure to give proper warnings was the causative nexus of [his] developing an irresistible gambling compulsion and thereby losing $12.2 million" in gambling losses. *Id.* ¶ 9; *see id.* ¶ 19.[6]

[6] Although Dr. Wells pled that he lost $12.2 million, Complaint ¶ 9, his recent discovery responses stated that it was $14 million. *See Plaintiff's Second Amended and Supplemental Disclosures* dated June 27, 2008 (Exhibit C).

1. Dr. Wells' history of gambling before taking Requip

Dr. Wells admitted that he had made regular gambling trips to Las Vegas since the 1980s, and, by the time his first symptoms of Parkinson's disease appeared, he had accounts at over a dozen casinos there. Wells Depo. Vol. 2, 75:17-77:8; 97:5-23. In 2000, soon after the diagnosis, but long before taking Requip, Dr. Wells had been increasing the amount of available credit in his casino accounts, but at that point, he still considered gambling to be social and recreational and did not feel his gambling was "out of control." Wells Depo. Vol. 3, 33:5-34:16.

In April 2001, Dr. Wells received a substantial amount of money from a partial sale of his interest in his pathology lab. Wells Depo. Vol. 3, 83:2-25; *see also Plaintiff's Response to Defendant SmithKline Beecham Corporation d/b/a GlaxoSmithKline's Second Interrogatories* ("Plaintiff's Interrogatory Response") at Nos. 1 & 2 (Exhibit D). That summer, shortly after starting another dopamine agonist, Mirapex (pramipexole), Wells Depo. Vol. 3, 77:9-12, Dr. Wells went on an Alaskan fishing cruise, complements of a Las Vegas casino. *Id.* 86:2-87:7.

During this same time-frame, Dr. Wells' Parkinson's disease symptoms worsened. In 2002, due to his disability, he stopped working in the demanding pathology practice that he had previously enjoyed and in 2003, due to the tremors, he had to give up his major pastime of building computers. Wells Depo. Vol. 4, 26:18-27:13. The disease did not, however, affect his ability to gamble. *Id.* at 27:10-12. Consequently, as to three activities he most enjoyed—work, building computers, and gambling—gambling was the only thing he could continue to do.

2. Dr. Wells changes from Mirapex to Requip

In May 2004, Dr. Wells told his treating physician, Sara A. Westgate, M.D., Ph.D ("Westgate"), of "increased gaming" and gave her an article reporting gambling in several Parkinson's disease patients who had taken Mirapex or pergolide, another medication for

Parkinson's disease. Wells Depo. Vol. 4, 43:15-18; 50:24-51:20 & Exhibit 26. Dr. Westgate reduced his Mirapex dose for one month, after which Dr. Wells contacted her to increase the dose to more effectively control his Parkinson's disease symptoms. Westgate Depo. at 144:14-22; 145:20-25; 155:22-156:2; 158:17-159:18. By September 2004, Dr. Wells reported "a major gambling problem" to Dr. Westgate. Wells Depo. Vol. 4 at 69:14-17; 70:2-12. By that point, Dr. Wells had lost somewhere between $1 to $2 million (although he did not report the amount to his doctor). *Id.* at 76:6-13; 95:1-4; Westgate Depo. at 177:9-15. In October 2004, Dr. Westgate discontinued Mirapex and prescribed Requip. Wells Depo. Vol. 4, 79:21-80:3. Dr. Wells alleges that his gambling subsided following the switch to Requip, but intensified again after his Requip dose was increased to better control his symptoms of Parkinson's disease. Wells Depo. Vol. 4; 87:13-19; Vol. 5, 12:19-25; 21:18-21; 25:13-26 and Exhibits 29 and 39.

In May 2005, Dr. Wells sold his remaining interest in his group medical practice and pathology lab and received an initial payment from the sale. Wells Depo. Vol. 5, 18:18-19:3. The day he received the sale proceeds, he went back to Las Vegas. *Id.* at 19:1-2; Plaintiff's Interrogatory Response at No. 2. By September 2005, he and his wife received another substantial payment from the sale, Wells Depo. Vol. 5, 21:24-22:16, and he took another trip to Las Vegas a week later. *Id.* at 22:18-23:14.

3. Dr. Wells stops gambling

In January of 2006, Dr. Wells totaled his gambling losses for the first time, and was shocked to discover that they were over $4 million in the past month alone. Wells Depo. Vol. 5, 41:14-42:3. He stated that, for the first time, he realized that "[g]ambling was going to drive [him] bankrupt" and told his wife how much he had lost. *Id.* 45:3-24. At that point, he told Dr. Westgate he "was having a problem gaming and it was a major problem and [he] needed to

do something." Wells Depo. Vol. 5, 44:7-12. He "told her more times in January that [he] was having major problems, there was something really wrong." *Id*. at 44:24-45:1. Dr. Westgate told him to decrease the Requip, and he discontinued it entirely on February 6, 2006. *Id.* at 46:19-48:7. Dr. Wells claims that he also stopped gambling, except for limited Internet gambling and the purchase of a lottery ticket, at the same time he stopped taking Requip. *Id.* at 48:20-49:4.

Less than two weeks after his Requip dose was discontinued, Dr. Wells commenced this lawsuit (in February 2006), and less than two months after he stopped taking Requip, he was evaluated in Los Angeles by two of his litigation experts. *See* Fong Report at 23 (Exhibit E); Kalechstein Report at 1 (Exhibit F).

B. Parkinson's Disease And Its Treatment

Parkinson's disease is a progressive, neurodegenerative disease of the brain that results from the loss of nerve cells. In addition to the motor symptoms of Parkinson's disease (tremor, slowness of movement, rigidity and shuffling gait), many Parkinson's disease patients have deficits in executive function (planning, judgment and insight); depression and anxiety are also common (Cummings Report[7] at 2-4) (Exhibit K).

Although Parkinson's disease is incurable, its symptoms can be treated with drugs that restore dopamine activity, known as dopaminergic drugs. Dopaminergic drugs act via a number of different mechanisms to produce their effects; they include drugs (*e.g.*, levodopa) that restore dopamine activity by increasing the brain's dopamine levels and other drugs, called dopamine agonists, that restore dopamine activity by directly stimulating one or more of five different

[7] "Cummings report" refers to the report of GSK's expert witness Jeffrey L. Cummings, M.D., Professor of Neurology and Psychiatry at UCLA, and a world-renowned expert behavioral neurologist.

types of dopamine receptors in the brain. Dopamine agonists include naturally-occurring ergot compounds like bromocriptine and pergolide, and synthetic non-ergot compounds like pramipexole (Mirapex) and ropinirole (Requip). Each dopamine agonist is a unique compound with a unique profile of pharmacologic activity (Cummings Report at 3; Grace report[8] at 4-5 (Exhibit L)).

C. Pathological Gambling

"Pathological gambling" is an impulse control disorder ("ICD") listed in the *Diagnostic & Statistical Manual of Mental Disorders – Fourth Edition – TR* ("DSM-IV-TR") of the American Psychiatric Association (Exhibit M).[9] No single characteristic, including the amount of money wagered or lost, is a necessary or sufficient condition for a diagnosis of pathological gambling. Instead, a diagnosis of pathological gambling requires that an individual meet five or more of ten specified criteria set forth in the DSM-IV-TR. These criteria are:

(1) is preoccupied with gambling (e.g., preoccupied with reliving past gambling experiences, handicapping or planning the next venture, or thinking of ways to get money with which to gamble)

(2) needs to gamble with increasing amounts of money in order to achieve the desired excitement

(3) has repeated unsuccessful efforts to control, cut back, or stop gambling

(4) is restless or irritable when attempting to cut down or stop gambling

(5) gambles as a way of escaping from problems or of relieving a dysphoric mood (*e.g.*, feelings of helplessness, guilt, anxiety, depression)

[8] "Grace report" refers to the report of GSK's expert witness Anthony A. Grace, Ph.D., Professor of Neuroscience, Psychology and Psychiatry at the University of Pittsburgh, and expert in dopamine receptors and pharmacology.

[9] "The essential feature of Impulse Control Disorders is the failure to resist an impulse, drive, or temptation not perform an act that is harmful to the person or others" (DSM-IV-TR at 663).

(6) after losing money gambling, often returns another day to get even ("chasing" one's losses)

(7) lies to family members, therapist, or others to conceal the extent of involvement with gambling

(8) has committed illegal acts such as forgery, fraud, theft, or embezzlement to finance gambling

(9) has jeopardized or lost a significant relationship, job, or educational or career opportunity because of gambling

(10) relies on others to provide money to relieve a desperate financial situation caused by gambling

(DSM-IV-TR at 674).[10]

"Problem gamblers" are those who meet three to four of the ten DSM criteria for pathological gambling. Up to 11.5% of the overall population are either problem gamblers or pathological gamblers during their lifetimes, and it is estimated that there are over one million problem and pathological gamblers in the State of Texas today (Petry Report[11] at 2) (Exhibit N). Risk factors for pathological gambling include, among other things, male gender, prior or current gambling, disability, chronic medical conditions, and prior or current depression or anxiety disorders. The

[10] Although Dr. Wells claims to have been a pathological gambler, his expert Dr. Fong, when asked which of the criteria for a diagnosis of pathological gambling Dr. Wells met during the period he was taking Requip, identified Nos. 1 (preoccupied with gambling) and 7 (lying to conceal extent of gambling), and possibly Nos. 8 (illegal acts to finance gambling – in Dr. Wells' case, taking money out of a joint account without his wife's knowledge) and 9 (jeopardizing relationships because of gambling) (Fong Depo. at 313:18-327:20). However, a diagnosis of pathological gambling requires that at least ***five*** criteria be present. *See* DSM-IV-TR at 674. Consistent with Dr. Fong's testimony, GSK disputes that Dr. Wells met the criteria for a diagnosis of pathological gambling during the period he took Requip or at any other time.

[11] "Petry report" refers to the report of GSK's expert witness Nancy M. Petry, Ph. D., a Professor in the Department of Psychiatry at the University of Connecticut School of Medicine and an internationally-recognized gambling expert. Dr. Wells' expert Dr. Fong has called Dr. Petry "certainly one of the most renowned gambling researchers in America and in the world" (Fong Depo. at 95:23-96:4) (Exhibit H).

most common triggers are depressed mood, unstructured time and access to money (*Id*. at pp. 2-3).

Despite knowledge about these various risk factors, very little is known about the specific causes or neurobiology of pathological gambling. For example, experts in the field do not know why some people have a gambling problem and others do not, what brain circuits are involved, how to prevent problem gamblers from becoming pathological gamblers, or how to predict who will become a pathological gambler, and it is not established that dopamine is the only neurotransmitter involved in pathological gambling (Fong Depo. at 192:20-193:5, 195:9-22, 196:23-25). In fact, pathological gamblers include people of both genders, all ages, all races, all walks of life and all income levels (*Id*. at 203:3-204:22). Moreover, problem and pathological gambling are known to wax and wane, no drug therapy is reliably effective in treating pathological gambling, there is a high placebo response rate in treatment studies, and a large proportion of pathological gamblers stop gambling without formal treatment, for a variety of emotional, financial or family reasons (Petry Report at 3-5; Fong Depo. at 194:1-25, 214:11-217:12).

ARGUMENT

I. There Is No Reliable Scientific Evidence That Requip Causes Pathological Gambling, And Any Such Testimony Would Therefore Be Inadmissible

As discussed at p. 2, *supra*, Dr. Wells must prove both general causation and specific causation. Establishing general causation would require methodologically-sound controlled studies documenting a statistically significant association between Requip and pathological gambling. As discussed below, there is no such study, and Dr. Wells' experts have conceded that they cannot point to any such study. Therefore, Dr. Wells cannot meet his burden of proof,

and any expert testimony as to general causation – *i.e.*, expert testimony that Requip causes pathological gambling – would be patently unreliable and inadmissible.

A. Dr. Wells Cannot Meet The Requirements Of *Daubert* And *Havner*

"Evidence of general causation must be provided in the form of expert testimony that satisfies the requirements of *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 125 L. Ed. 2d 469, 113 S. Ct. 2786 (1993) and Rule 702 of the Federal Rules of Evidence." *In re Norplant Contraceptive Prods. Liab. Litig.*, 215 F. Supp. 2d 795, 830 (E.D. Tex. 2002). The U.S. Supreme Court held in *Daubert* that Federal Rule of Evidence 702 imposes a "gatekeeping" obligation, requiring trial courts to screen proffered expert testimony to ensure that such testimony is both reliable and relevant before it may be admitted at trial. 509 U.S. at 589-92, 113 S. Ct. at 2795-96; *Tanner v. Westbrook*, 174 F.3d 542, 545 n.1 (5th Cir. 1999) ("*Daubert* requires that when expert testimony is offered, the trial judge must perform a screening function to ensure that the expert's opinion is reliable and relevant to the facts at issue in the case"). In *Daubert*, the Supreme Court provided a non-exhaustive list of factors for the courts to consider in determining whether evidence is scientifically valid and reliable. These include: (i) whether the expert's theory has or can be tested; (ii) whether the theory has been subject to peer review and publication; (iii) the known or potential rate of error of a technique or theory when applied; (iv) the existence and maintenance of standards and controls; and (v) the degree to which the technique or theory has been generally accepted in the scientific community. 509 U.S. at 593-94, 113 S. Ct. at 2796-97.

Trial courts must also screen expert opinion testimony to determine whether the testimony is based on reliable data ***and*** supported by the data on which the expert relies. As the Texas Supreme Court explained in *Havner*:

> If the foundational data underlying opinion testimony are unreliable, an expert will not be permitted to base an opinion on that data because any opinion drawn from that data is likewise unreliable. Further, an expert's testimony is unreliable even when the underlying data are sound if the expert draws conclusions from that data based on a flawed methodology. A flaw in the expert's reasoning from the data may render reliance on a study unreasonable and render the inferences drawn therefrom dubious. Under that circumstance, the expert's scientific testimony is unreliable and, legally, no evidence. (953 S.W.2d at 714).[12]

Havner sets forth specific requirements that must be met in order for expert testimony based on epidemiological data to have an adequate foundation, such that it may be admitted as proof of causation, each of which will be addressed in turn below.

1. The data must be statistically significant

To support an opinion as to causation, there must be a valid study showing a statistically significant association between exposure to a product or other substance and an injury or other condition. *See Havner*, 953 S.W.2d at 723-24; *Frias v. Atlantic Richfield Co.*, 104 S.W.3d 925, 930 (Tex. App—Houston 2003); *Exxon Corp. v. Makofski*, 116 S.W.3d 176, 183 (Tex. App—Houston 2003); *see also Brock v. Merrell Dow Pharm., Inc.*, 884 F.2d 166, 167 (5th Cir. 1989) ("We find, in this case, the [plaintiffs'] failure to present statistically significant epidemiological proof that Bendectin causes limb reduction defects to be fatal to their case."). In order for the findings in a study to be statistically significant, the "confidence interval" must not include 1.0.

[12] *Havner* incorporated the admissibility standards of *Daubert* and *E.I. DuPont de Nemours & Co. v. Robinson*, 923 S.W.2d 549, 558 (Tex. 1995) into the standard governing review of verdicts for legal sufficiency. *See Havner*, 953 S.W.2d at 714. Because the legal sufficiency issue is substantive, *Havner* applies to federal court diversity cases like this one in which Texas law applies. *See, e.g., Cano v. Everest Minerals Corp.*, 362 F. Supp. 2d 814, 822 (W.D. Tex. 2005). And because the decision whether to admit expert testimony "is governed in part by whether the testimony is relevant to the plaintiff's burden of proof under the substantive law," the same factors that govern a court's decision of the legal sufficiency issue under *Havner* also govern the admissibility issue under *Daubert*. *Id*. at 821-22.

"A confidence interval shows 'a range of values within which the results of a study sample would be likely to fall if the survey were repeated numerous times.'" *Havner*, 953 S.W.2d at 723. "The generally accepted significance level or confidence level in epidemiological studies is 95% . . . ." *Id.* Under *Havner*, a study must have a confidence interval that does not include 1.0, at a confidence level of at least 95%, before an expert may rely on the study to support an opinion as to causation.[13]

Dr. Wells' experts all have conceded that no study reports a statistically significant association between treatment with Requip and pathological gambling:

- Dr. Fong testified as follows:

  Q: . . . based on your review of the literature, can you identify a single study that reports a statistically significant association between Requip and any level of gambling?

  A: A statistically significant association?

  Q: Yes.

  A: No, I cannot. (Fong Depo. at 161:16-22.)

- Dr. Kalechstein testified as follows:

  Q: Okay. Can you identify for me a single study that reports a statistically significant association between Requip and pathological gambling?

  A: No. The studies that I've reviewed use a case approach to addressing that. (Kalechstein Depo. at 110:25-111:4.)

[13] Other courts have addressed statistical significance in terms of a different but related measure called the "probability" or "*p*" value. The conventional criterion for statistical significance is a p value <0.05, which means that the probability that the association observed is due to chance is less than 5 percent. *See Wade-Greaux v. Whitehall Labs., Inc.*, 874 F. Supp. 1441, 1452 (D.V.I.), *aff'd*, 46 F.3d 1120 (3d Cir. 1994).

* * *

Q: (BY MS. BENNES) So you cannot identify for me a single study that shows a statistically significant association between Requip and gambling – or pathological gambling?

MR. MADRID: Objection; form.

A: I cannot. (*Id*. at 113:21-114:1.)

- Dr. Saklad testified as follows:

Q: You don't believe ropinirole is capable of causing pathological gambling?

A: No. I don't believe that the causation is proven. My distinction between association and causation is that causation requires scientific literature that proves a statistically valid reproducible result which could be used to establish causation. Such studies have not been done. (Saklad Depo. at 43:4-11.)

By Dr. Wells' experts' own admissions, the requirement for data showing a statistically significant association cannot be met in this case.

2. The data must show a doubling of the risk

Because a plaintiff's burden of proof is "more likely than not," epidemiological evidence generally cannot support an opinion as to causation unless the evidence shows that exposure to the substance at issue at least doubles the risk of the condition claimed to be associated with such exposure. *See Havner*, 953 S.W.2d at 715-17. Stated otherwise, it cannot be said that a condition is "more likely than not" caused by an exposure unless the occurrence of the condition in persons exposed is at least double the relevant background rate. *See id.* at 717-18.

The risk of injury related to exposure is the "relative risk." *See Brock v. Merrell Dow Pharm., Inc*., 874 F.2d 307, 312 (5th Cir.) ("The relative risk is a number which describes the

increased or decreased incidence of the disease in question in the population exposed to the factor as compared to the control population not exposed to the factor"), *modified on reh'g*, 884 F.2d 166 (5th Cir. 1989).[14] *Havner* requires a relative risk of at least 2.0 that is statistically significant before an epidemiological study may be accepted as the basis for an opinion as to causation. *See Cotroneo v. Shaw Environmental & Infrastructure, Inc.*, Civ. No. H-05-1250, 2007 U.S. Dist. LEXIS 79139, at *14-15 (S.D. Tex. Oct. 25, 2007) (opinion based on epidemiological studies that did not show doubling of risk "is insufficient to create a genuine issue of material fact on causation"); *Exxon Corp. v. Makofski*, 116 S.W.3d at 184 (study showing relative risk of 1.32 held legally insufficient under *Havner*); *Daniels v. Lyondell-Citgo Refining Co. Ltd.*, 99 S.W.3d 722, 730 (Tex. App—Houston 2003) (affirming summary judgment for defendant although plaintiffs' experts relied on three epidemiological studies; "None of the studies has the *Havner* requisite risk-doubling . . . ."); *Allison v. Fire Ins. Exchange*, 98 S.W.3d 227, 239 (Tex. App—Austin 2002) (affirming order excluding causation testimony based on study that did not "show that exposure to the substance more than doubles the risk of injury").

As noted above, Dr. Wells' experts all have conceded that no study shows a statistically significant association between treatment with Requip and pathological gambling, much less a doubling of the risk of that condition in patients so treated. Indeed, the one controlled study that specifically examined a possible association between Requip and pathological gambling reported an odds ratio – 1.13 – less than the 2.0 odds ratio required under *Havner*; in addition, that study did not report a statistically significant association—the confidence interval (0.11-12.13)

[14] Depending on the type of study from which the data are derived, the increased incidence of a condition may be expressed in terms of "odds ratio" rather than relative risk. *See Reference Manual on Scientific Evidence* 350 (Federal Judicial Center, 2d ed. 2000).

included 1.0. *See* Imamura A *et al.* Medications used to treat Parkinson's disease and the risk of gambling. *Eur. J. Neurol.* 2008, 15:350-54 (Exhibit R Kelder Report[15] at 11 (Exhibit O). ***Accordingly, the Havner risk-doubling requirement cannot be met in this case.***

3. The study must involve the same substance and injury

"To raise a fact issue on causation and thus to survive legal sufficiency review, a claimant must do more than simply introduce into evidence epidemiological studies that show a substantially elevated risk. A claimant must show that he or she is similar to those in the studies." *Havner*, 953 S.W.2d at 720. "This would include proof that the injured person was exposed to the same substance [and] that the exposure or dose levels were comparable to or greater than those in the studies . . . ." *Id*.; *accord Exxon Corp. v. Makofski*, 116 S.W.3d at 184-85 (rejecting opinion concerning effects of benzene exposure based on study finding association between leukemia and exposure to benzene and *other* solvents; the study "tells us nothing definitive" about association with benzene alone); *Daniels v. Lyondell-Citgo Refining Co., Ltd.*, 99 S.W.3d at 729 (affirming summary judgment for defendants based on *Havner*; plaintiff who claimed lung cancer caused by exposure to benzene could not rely on studies involving exposure to hydrocarbons that "did not specifically address benzene"); *see also Knight v. Kirby Inland Marine, Inc.*, 363 F. Supp. 2d 859, 864-65 (N.D. Miss. 2005) (excluding expert opinion based in part on studies of "individuals exposed to a broad class of organic solvents," including solvents to which the plaintiff was not exposed), *aff'd*, 482 F.3d 347 (5th Cir. 2007).[16]

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[15] "Kelder report" refers to the report of GSK's expert witness Steven H. Kelder, Ph.D., Professor of Epidemiology at the University of Texas Health Center, Austin Regional Campus.

[16] The requirement that the plaintiff be exposed to the same substance is especially important in cases involving drugs because it is axiomatic that "[r]elatively minor modifications to the drug molecule may result in major changes in pharmacological properties." Goodman & Gilman, *The Pharmacological Basis of Therapeutics* 32 (10th ed. 2001) (Exhibit Q); *see, e.g., McClain v.*

Besides showing that he was exposed to the same substance as the study subjects, a plaintiff relying on epidemiological evidence must show that he experienced the same injury or other condition as those subjects. *See, e.g., Knight v. Kirby Inland Marine*, 363 F. Supp. 2d at 864 (excluding expert's opinion that was based in part on studies that "failed to provide a risk factor for Hodgkin's disease [the injury claimed by plaintiff] apart from other lymphomas and myelomas"); *Current v. Atochem North America, Inc.*, Civ. No. W-00-CA-332, 2001 U.S. Dist. LEXIS 26239, at *11 (W.D. Tex. Nov. 30, 2001 (excluding expert testimony that arsenic causes rectal cancer, based on studies that "are only relevant for the proposition that arsenic exposure can cause lung and/or urinary cancers"); *Exxon Corp. v. Makofski*, 116 S.W.3d at 184-85 (rejecting opinion based on study finding association with leukemias other than the one claimed).

Dr. Wells claims that he developed pathological gambling as the result of his treatment with Requip. Yet, as discussed above, Dr. Wells' experts have conceded that no study shows a statistically significant association between the same substance to which he was exposed—***Requip***—and the same injury he allegedly suffered—***pathological gambling***. ***Accordingly, the same substance/injury requirements cannot be met in this case.***

4. Case reports cannot support an opinion as to causation

A "case report" is simply a report concerning a particular patient or "case." Because a case report is an uncontrolled anecdotal observation regarding a patient, case reports are only hypothesis-generating, and no inferences as to causation may be drawn from them. *See Havner*, 953 S.W.2d at 719-20 ("Courts should . . . reject such evidence because it is not scientifically reliable"). Other courts have, on the same basis, found expert opinions based on case reports

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Metabolife Int'l Inc., 401 F.3d 1233, 1245 (11th Cir. 2005) (district court erred in admitting expert testimony that defendant's product could damage blood vessels where testimony was based on analogy to other drug; "[s]peculation replaces science in this unreliable analogy").

scientifically unreliable and inadmissible under *Daubert*. *See, e.g., Castellow v. Chevron USA*, 97 F. Supp. 2d 780, 787 (S.D. Tex. 2001) (attempts to form opinions regarding causation based on case reports or collections of case reports "'are unscientific and speculative'").[17]

Most of the scientific literature regarding dopamine agonists and pathological gambling consists of case reports (*see* Kelder Report at 13-14), and Dr. Wells' experts rely heavily on such reports for their opinion that Requip caused Dr. Wells' claimed pathological gambling. *See, e.g.*, Kalechstein Depo. at 110:25-111:6; Saklad Report at Appendix 3. ***Such reports are legally insufficient under the above authorities and scientifically inadequate to establish causation, as Dr. Fong has acknowledged***. *See* Fong Depo. at 62:14-16 ("Q. . . . a case report can't establish a cause-and-effect relationship, can it? A. No, it cannot").

5. A statistically significant association is only the first step in proving causation

Although results from a valid study showing a statistically significant association and a doubling of the risk are generally required, such data are not by themselves sufficient to prove causation. *See Havner*, 953 S.W.2d at 724 ("It must be reiterated that even if a statistically significant association is found, that association does not equate to causation"). Epidemiologists apply certain criteria known as the Bradford-Hill criteria to make a determination as to causation, but these criteria are applied only ***after*** a statistically significant association has been identified. Conclusions about causation may not be drawn until these criteria have been considered. *Id*. at

[17] For the same reason that case reports cannot support an opinion as to causation – namely, because they are uncontrolled anecdotal observations, a clinician's experience and adverse event reports to regulatory authorities likewise are not scientifically-reliable bases for an opinion as to causation. *See, e.g., Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 887 (10th Cir. 2005) ("We cannot allow the jury to speculate based on an expert's opinion which relies only on clinical experience in the absence of showing a consistent, statistically-significant association . . . ."); *Brumbaugh v. Sandoz Pharm. Corp.*, 77 F. Supp. 2d 1153, 1157 (D. Mont. 1999) (adverse event reports "are compilations of occurrences, and have been rejected as reliable scientific evidence supporting expert opinion so as to meet the requirements set forth in *Daubert*").

718; *Dunn v. Sandoz Pharm. Corp.*, 275 F. Supp. 2d 672, 678 (M.D.N.C. 2003) (an association is the `starting point' of [the Bradford-Hill] criteria"); *Soldo v. Sandoz Pharm. Corp.*, 244 F. Supp. 2d 434, 461 (W.D. Pa. 2003) ("application of the Bradford Hill criteria depends first upon an association by epidemiology between a disease and an exposure to an agent").[18]

Because there are no data showing a statistically significant association between Requip and pathological gambling, there is no basis even to apply the criteria that are used to determine whether such an association, once established, is a causal association (Kelder Report at 14).

For these and other reasons, as explained further in Dr. Kelder's report, even if Dr. Wells' experts were prepared to testify that Requip causes pathological gambling (which they are not), any such opinion would not meet the requirements of Daubert and Havner, and therefore would be scientifically unreliable and inadmissible.

B. It Is Not Generally Accepted That Requip Causes Pathological Gambling

As noted previously, general acceptance is one of the criteria the *Daubert* Court directed trial courts to apply in determining whether proposed expert testimony is admissible. *See, e.g.*, *Knight v. Kirby Inland Marine, Inc.*, 482 F.3d 347, 355 (5th Cir. 2007) (affirming order excluding testimony by expert whose causation theory was not supported by statistically significant evidence and "not generally accepted"); *Kelley v. American Heyer-Schutte Corp.*, 957 F. Supp. 873, 879 (W.D. Tex. 1997) (excluding testimony based on reanalysis of data using methodology that was not generally accepted), *app. dism'd*, 139 F.3d 899 (5th Cir. 1998).

Consistent with Dr. Wells' experts' testimony that causation is not established, it is not generally accepted in the scientific community that Requip causes pathological gambling. For

[18] Although they claimed to know enough about epidemiology to evaluate epidemiological studies, neither Dr. Fong nor Dr. Kalechstein had heard of the Bradford-Hill criteria. *See* Fong Depo. at 60:9-11; Kalechstein Depo. at 88:19-23.

example, as recently as December 2007, three authors who had previously published studies examining a possible relationship between dopamine agonists and pathological gambling published a review article summarizing the scientific literature. *See* Potenza M *et al.* "Drug Insight: impulse control disorders and dopamine therapies in Parkinson's disease. *Nature* 2007; 3(12):664-72 (Exhibit S). Although the authors pointed to "mounting evidence indicat[ing] that the occurrence of ICDs in patients with PD [Parkinson's disease] ***might be associated*** with dopamine agonist treatment" (*id*. at 664; emphasis added), they did ***not*** conclude that such treatment causes pathological gambling or other ICDs, as Dr. Fong acknowledged (*see* Fong Depo. at 171:11-13). The authors instead acknowledged the presence of various confounding factors, noting for example that "the stress of coping with a chronic medical illness might contribute to the development of an ICD" and that "[t]he extent to which ICDs co-occur with other psychiatric disorders that are observed in association with PD (e.g., dementia) has not been systematically evaluated." Potenza M *et al.* at 665-66. The authors also noted that the "association between PDs and ICDs could theoretically be related to the pathophysiology of PD, interventions used to treat PD, or a combination of the two." *Id*. at 666. The authors concluded that the specific factors underlying the observed association between dopamine agonist therapy and ICDs "remain unclear" and that "[p]rospective, longitudinal studies comparing subjects before or at PD onset with appropriate control groups will be important for improving our understanding of the prevalence and treatment of ICDs in PD." *Id*. at 649. In an even more recent review article published in March 2008, Drs. Stamey and Jankovic, from the Parkinson's Disease Center and Movement Disorders Clinic at the Baylor College of Medicine, made similar observations. *See* Stamey W and Jankovic J. Impulse Control Disorders and Pathological Gambling in Patients with Parkinson Disease. *The Neurologist* 2008; 14(2):89-99 (Exhibit U).

They noted that "[t]he true prevalence of PG [pathological gambling] in patients with PD is not known and currently applied methods do not provide accurate estimates," *id*. at 90, and that "[w]hether PD alone or in combination with dopaminergic therapy results in ICD and PG is still not entirely clear . . . . *Id*. at 92.

As these recent review articles demonstrate, the existence of any relationship between dopamine agonist treatment and ICDs, much less one between Requip and pathological gambling, is an "open question." Absent general acceptance that Requip causes pathological gambling, any opinion as to general causation would be scientifically unreliable and inadmissible.

II. The Specific Causation Opinions Of Dr. Wells' Experts Are Scientifically Unreliable And Therefore Inadmissible

Because Dr. Wells' experts cannot present scientifically-reliable opinions as to general causation, the Court need not consider whether his experts' opinions as to specific causation are admissible. *See, e.g., Knight v. Kirby Inland Marine Inc.*, 482 F.3d at 351 ("Evidence concerning specific causation in toxic tort cases is admissible only as a follow-up to admissible general causation evidence."); *Anderson v. Bristol Myers Squibb Co.*, No. Civ. A. H-95-0003, 1998 U.S. Dist. LEXIS 23259, at *23 (S.D. Tex. Apr. 17, 1998); *Kelley v. American Heyer-Schutte Corp.*, 957 F. Supp. at 882. Dr. Wells' experts' opinions as to specific causation – that Requip caused his claimed pathological gambling – must in any event be excluded because they do not have a reliable scientific basis. In addition, Dr. Saklad is not qualified to render an opinion as to specific causation, and his specific causation opinion based solely on the allegations in the Complaint is scientifically unreliable.

A. Dr. Wells' Experts Improperly Base Their Opinions on the Claimed Temporal Relationship Between His Treatment with Requip And Increased Gambling And Ignore Other Factors That May Have Accounted For Dr. Wells' Gambling

Dr. Wells' experts base their opinions that his claimed pathological gambling[19] was caused by Requip on their statements that, except for his treatment with dopamine agonists, Dr. Wells had no risk factors for pathological gambling. *See* Fong Report at 31-32 (Dr. Wells "did not carry any of the primary risk factors for pathological gambling"); Kalechstein Report at 35 (Dr. Wells had "no other mental health conditions, mental disorders, acute conditions, or historical factors that could account for the onset of the gambling behavior"). Having identified no other risk factors in their reports,[20] Dr. Wells' experts conclude that his claimed pathological gambling ***must*** have been caused by Requip because his gambling increased after he started taking Requip. *See* Fong Report at 32 (Dr. Wells' "pathological gambling symptoms emerged only AFTER initiation of dopamine agonist" [emphasis in original]); Kalechstein Report at 34 ("[T]he dates on which he took Requip was [*sic*] consistent with the timeframe in which his gambling behavior changed."); Saklad Report at 3 ("Subsequent to the ropinirole's titration to an effective dose, Dr. Wells' compulsive gambling worsened.").

The claimed temporal relationship between Dr. Wells' treatment with Requip and his increased gambling is not a proper basis for an opinion as to specific causation. *See, e.g.*, *McClain v. Metabolife Int'l, Inc.*, 401 F.3d at 1243 ("[D]rawing such a conclusion from temporal relationships leads to the blunder of the *post hoc ergo propter hoc* [after the fact, therefore because of the fact] fallacy."); *Moore v. Ashland Chem. Inc.*, 151 F.3d 269, 278 (5th Cir. 1998)

[19] As noted in footnote 10 at p. 10 *supra*, Dr. Fong effectively withdrew the pathological gambling diagnosis at his deposition.

[20] As discussed below, Dr. Fong conceded at his deposition that Dr. Wells in fact had several risk factors that could have contributed to his increased gambling.

("[T]he temporal connection between exposure to chemicals and an onset of symptoms, standing alone, is entitled to little weight in determining causation."); *Wooley v. Smith & Nephew Richards, Inc.*, 67 F. Supp. 2d 703, 708 (S.D. Tex. 1999) (rejecting "generic conclusion" based on temporal connection); *Schmaltz v. Norfolk & Western Ry. Co.*, 878 F. Supp. 1119, 1122 (N.D. Ill. 1995) ("It is well settled that a causation opinion based solely on a temporal relationship is not derived from the scientific method and is therefore insufficient to satisfy the requirements of FED R. EVID. 702.").

Furthermore, in identifying Dr. Wells' treatment with Requip as the only factor that could explain his increased gambling (because he purportedly had no other "primary risk factors"), Dr. Wells' expert witnesses ignore that fact that Dr. Wells had ***numerous*** established risk factors for problem or pathological gambling – risk factors that include history of gambling, chronic illness, disability and history of depression and anxiety disorders (Petry Report at 2-3)—***prior*** to his treatment with Requip:

- Dr. Wells had a history of depression, as well as depressed mood, anxiety and stress (Fong Report at 30; Fong Depo. at 303:11-17; Kalechstein Report at 9; Petry Report at 10-11); Dr. Fong testified that he could not rule out Dr. Wells' past depression as a risk factor for increased gambling and that the stress of coping with a chronic illness might contribute to development of an ICD (Fong Depo. at 174:20-175:6, 304:11-24).
- Dr. Wells had a significant history of gambling that increased in the 1990s, prior to his diagnosis of Parkinson's disease, and continued to increase prior to his treatment with Requip (*see* p. 6, *supra*); Dr. Fong acknowledged that a prior history of problem gambling is a risk factor for pathological gambling (Fong Depo. at 205:7-9).

- Dr. Wells was diagnosed with Parkinson's disease, a disabling, neurodegenerative disease, in 2000, and as a result of that disease, he was fully disabled by 2002 (*see* p. 6 *supra*); Dr. Fong acknowledged that "Dr. Wells' disability in and of itself is a – is a risk factor for developing pathological gambling" (Fong Depo. at 280:19-281:5).
- As a result of his inability to practice medicine, Dr. Wells sold his interest in his medical practice and lab, for which he and his wife received a significant amount of money (*see* pp. 6-7 *supra*). Thus, Dr. Wells had substantially more time and money available to him, and gambling was the one preferred activity he could still pursue; Dr. Fong acknowledged that Dr. Wells' receipt of such a large sum of money might have played a role in his increased gambling (Fong Depo. at 260:20-23).

Any opinion that Requip caused Dr. Wells' increased gambling must consider and exclude these risk factors. Because Dr. Wells' experts did not even mention, much less consider and exclude, these factors in their reports, the opinions in those reports are unreliable and inadmissible. *See Havner*, 953 S.W.2d at 720 ("[I]f there are other plausible causes of the injury or condition that could be negated, the plaintiff must offer evidence excluding those causes with reasonable certainty."); *Rowan Companies Inc. v. Acadian Ambulance Service, Inc.*, No. H-05-3400, 2008 WL 1989791, at *12 (S.D. Tex. May 2, 2008) (excluding testimony of expert who "fail[ed] to identify much less rule out, eliminate or take exception to other risk factors that may have contributed" to the plaintiff's injuries); *Cano v. Everest Minerals Corp.*, 362 F. Supp. 2d at 840 ("An expert who fails to scientifically rule out or quantify alleged risk factors to arrive at the most likely cause offers a specific causation opinion that is nothing more than pure speculation"); *Merck & Co., Inc. v. Ernst*, No. 14-06-00835-CV, 2008 WL 2201769, at *5-6 (Tex. App—Houston May 29, 2008) (absent support in the scientific literature, expert witness'

testimony that decedent lacked other risk factors for cardiovascular disease did not support his conclusion that defendant's product caused decedent's cardiovascular event).[21]

B. Dr. Wells' Experts Improperly Ignore Other Factors That May Have Accounted For Dr. Wells' Claimed Cessation Of Gambling

In addition to basing their opinions on the claimed absence of other risk factors and the temporal relationship between Dr. Wells' increased gambling and his treatment with Requip, Dr. Wells' experts all rely on the fact that his claim that he stopped gambling at the same time he stopped taking Requip in early 2006. *See* Fong Report at 31-32 (Dr. Wells' "pathological gambling symptoms . . . all resolved AFTER discontinuation of dopamine agonists." [emphasis in original]); Kalechstein Report at 34-35 (Dr. Wells "has not demonstrated aberrant gambling behavior since he discontinued his prescription of Requip."); Saklad Depo. at 38:10-23 (specific causation opinion is based on "the time course and the dose response relationship that was evident in Dr. Wells").

In fact, contrary to his experts' analysis, the discontinuation of Requip was ***not*** the only relevant event that coincided with the claimed cessation of Dr. Wells' gambling. Problem and pathological gambling are characterized by a waxing and waning course, and a majority of

[21] In addition to being legally insufficient under these authorities, Dr. Wells' experts' opinions are scientifically unreliable because they are based on the assumption that the causes of pathological gambling are so clearly defined and established that one can arrive at ***the*** cause of an individual's gambling by excluding other causes. That assumption is erroneous because, as Dr. Fong testified, people from all walks of life become pathological gamblers for reasons experts in the field, including himself, cannot determine or predict (Fong Depo. at 192:20-193:5; 202:25-204:22). Thus, because pathological gambling often has no known cause, even if it were clear that Dr. Wells was at some point a pathological gambler (which GSK denies), neither Dr. Fong nor anyone else could logically arrive at a single cause for Dr. Wells' gambling through a process of excluding other known causes. *See Perry v. Novartis Pharm. Corp.*, Civ. No. 05-5350, slip op. at 31-32 (E.D. Pa. Jul. 9, 2008) (specific causation opinions properly excluded where they "fail[] to adequately account for the likelihood that the disease was caused by an unknown factor").

pathological gamblers who stop gambling do so without formal treatment, for emotional, financial and family reasons. In addition, pathological gamblers frequently stop or reduce gambling once they recognize their problem, as confirmed by treatment studies that show high rates of response to minimal or no interventions and placebo response rates of 50% or more. *See* Petry N. *Pathological Gambling* 142, 153-56 (Amer. Psychol. Assn. 2005); Petry Report at 3-5. Thus, in the present case, Dr. Wells' cessation of gambling corresponded in time, not only to the discontinuation of Requip, but also to Dr. Wells' own tallying up of his gambling losses, his realization that he could go bankrupt if he continued to gamble, telling his wife how much he had lost, and repeatedly telling his doctor that he was having "major problems." Moreover, having filed this lawsuit less than two weeks after he stopped taking Requip, Dr. Wells was motivated to refrain from further gambling in order to advance the claim that his gambling was caused by Requip and to avoid the embarrassment he felt when his lawsuit was reported in the newspaper (Petry Report at 11-12).

Dr. Fong acknowledged many of these points during his deposition. He testified that 20% to 40% of pathological gamblers recover spontaneously, without treatment, often because of an "inciting event" or—in more colloquial terms—a "why now moment" (Fong Depo. at 214:14-215:2, 216:22-217:12, 218:3-20), and he agreed "absolutely" that Dr. Wells' recognition that he could go bankrupt if he continued to gamble was just such a "why now" moment for him (*Id*. at 270:19-271:18). Moreover, although the discontinuation of Requip was the only event Dr. Fong listed in his report as corresponding in time with Dr. Wells' cessation of gambling, at his deposition he amended his report "to put in other additional contributing – possible contributing factors to why he stopped gambling":

> I would include No. 1, possibility that he did file a lawsuit and stopped it – and stopped gambling to support the lawsuit. Number two, that the shame and guilt he experienced from the newspaper and the humiliation of that was enough to trigger – to help him, motivate him to stop gambling.
>
> No. 3, the awareness of his wife knowing that – how much he lost gambling may have also served as a contributing factor. No. 4, the actual act of adding up gambling losses would be enough to – could serve as a possible contributing factor to helping him, again, assist in stopping his gambling (*Id*. at 300:5-301:3).

In summary, and as Dr. Fong's testimony confirms, Dr. Wells' experts' specific causation opinions are not scientifically reliable because they are based on the temporal relationship between Dr. Wells' increased gambling and his treatment with Requip and fail to take into account a number of other uncontroverted and relevant factors that may explain Dr. Wells' increased gambling and its later cessation.

C. Dr. Saklad Is Not Qualified to Express An Opinion As To Specific Causation

Even if Dr. Wells' proposed expert testimony as to specific causation were otherwise admissible, which it is not, any such testimony by Dr. Saklad should be precluded because he is not qualified to testify regarding the claimed cause of Dr. Wells' increased gambling. Federal Rule of Evidence 702 requires that an expert witness be qualified by virtue of his "knowledge, skill, experience, training or education." "A district court should refuse to allow an expert witness to testify if it finds that the witness is not qualified to testify in a particular field or on a given subject." *Wilson v. Woods*, 163 F.3d 935, 937-38 (5th Cir. 1999) (citation omitted) (affirming decision excluding testimony of purported accident reconstruction expert who "had never taught accident reconstruction courses, never experienced or conducted studies in the field, and never published anything on that subject").

First and foremost, Dr. Saklad is not a medical doctor or a mental health professional. His license as a pharmacist does not authorize him to make medical or psychiatric diagnoses (Saklad Depo. at 84:4-85:6) or to prescribe medication. In fact, Dr. Saklad admitted that he is not qualified to diagnose pathological gambling and that he has authored no publications regarding pathological gambling, Requip, or other drugs used to treat Parkinson's disease (*Id*. at 114:7-11, 169:4-15). Even physicians are not permitted to testify about matters outside their areas of expertise and experience. *See, e.g., Cleveland v. United States*, 457 F.3d 397, 405 (5th Cir. 2006) (specialist in internal medicine not qualified to testify to standard of care for diagnosing congestive heart failure in emergency room setting). It follows *a fortiori* that Dr. Saklad, a pharmacist who admits he is not an expert on pathological gambling, is not qualified to address the cause of Dr. Wells' gambling. Moreover, given his lack of relevant experience, it is apparent that Dr. Saklad's claimed knowledge regarding Parkinson's disease, dopamine agonists, pathological gambling and other pertinent matters is precisely "the sort of 'litigation-drive[n] expertise' which courts have eschewed." *DeVito v. Smithkline Beecham Corp.*, No. Civ. A. 02-CV-0745NPM, 2004 U.S. Dist. LEXIS 27374, at *25 (N.D.N.Y. Nov. 29, 2004); *Liner v. Davol, Inc.*, No. 97-60808, 1999 WL 129846, at *2 (5th Cir. Feb. 11, 1999) (board-certified physician not qualified to render opinion regarding medical device he never used and as to which he "never conducted any research into the academic literature . . . outside the context of this lawsuit")

Dr. Saklad's specific causation opinion is all the more lacking in scientific basis because it is premised, by Dr. Saklad's own admission, not on his review of medical records, testimony or other evidence, but solely on the allegations in the Complaint filed by Dr. Wells' counsel (Saklad Depo. at 37:19-38:23). This is not a proper basis for an expert opinion. *See Stinson Air*

Ctr., LLC v. *XL Specialty Ins. Co*., No. Civ. SA-03-CA-61-FB, 2005 WL 5979095, at *3 (W.D. Tex. Jul. 8, 2005) ("Because [the expert's] proposed opinion . . . was based solely upon representations of a party with an interest in the outcome of this lawsuit . . . this court finds [the expert's] methodology for formulating this specific expert opinion to be unorthodox and unreliable"). Dr. Saklad admitted that it is not his usual methodology to base his review of patients' medical histories on legal documents (Saklad Depo. at 134:17-135:8), and he testified further that "if I was looking for drug-induced pathological gambling, I would want to know the gambling history compared to after the drug is started" (*Id*. at 143:8-11). But Dr. Saklad ***admitted that he did not have this information*** (*id*.); indeed, because he relied solely on the information in the Complaint, Dr. Saklad lacked ***any*** information concerning key facts bearing on Dr. Wells' gambling, including the "comps" Dr. Wells was receiving from Las Vegas casinos even before he took Mirapex; the fact that Dr. Wells and his wife received a substantial amount of money the month before he claims his gambling began to increase; the activities Dr. Wells most enjoyed before his illness and the effect his illness had on those activities (other than gambling); and the circumstances that surrounded the cessation of Dr. Wells' gambling (*Id*. at 145:1-146:16). There is simply no way that a purported expert witness—even a witness (unlike Dr. Saklad) with appropriate qualifications—could provide scientifically-reliable testimony regarding the cause of Dr. Wells' gambling without this information.

III. Dr. Saklad Is Not Qualified To Express An Opinion Regarding The Adequacy Of The Requip Labeling

A. Dr. Saklad Is Not Qualified To Opine Concerning Prescription Drug Labeling

Dr. Saklad has absolutely no experience in prescription drug regulation or labeling: Dr. Saklad never worked for the FDA, he has no training in this field (Saklad Depo. at 197:18-

21); he has never published or given a presentation focusing on prescription drug labeling (*id*. at 197:22-198:9); he has never written a regulation pertaining to prescription drugs (*id*. at 193:25-194:1); he has never drafted labeling for a prescription drug (*id*. at 195:13-15); and he has never commented on a proposed regulation pertaining to when a warning should be added to labeling (*Id*. at 194:19-23). Dr. Saklad further admits that, although there are professionals who specialize in writing and evaluating labeling for prescription drugs, he is not one of them. *Id.* at 191:25-192:5.

This is the first case in which Dr. Saklad has ever expressed an expert opinion regarding a company's failure to warn, or written a report or testified about the adequacy of warnings for a drug approved by the FDA. Saklad Depo. at 62:15-18, 63:21-24. Indeed, at the time Dr. Saklad agreed to provide an expert opinion in this case, ***he had never even read the applicable regulation*** governing prescription drug labeling, even though he acknowledged that "the regulation is what I was basing my opinion on." *Id*. at 183:11-184:6, 184:16-24. Dr. Saklad is plainly unqualified to express an opinion with respect to the adequacy of the Requip labeling, and his testimony on this issue should be precluded. *See, e.g., Wehling v. Sandoz Pharms. Corp.*, No. 97-2212, 1998 U.S. App. LEXIS 38866 (4th Cir. Aug. 20, 1998) (affirming order finding pharmacist-toxicologist unqualified to testify as to drug label's adequacy); *DeVito v. Smithkline Beecham Corp.*, 2004 U.S. Dist. LEXIS 27374, at *33-34 (excluding testimony as to drug labeling by pharmacist who "has never been a drafter or been asked to draft a warning for any antidepressant" and "has not done any research or written any publications on prescription drug warnings"); *In re Rezulin Prods. Liab. Litig.*, 309 F. Supp. 2d 531, 548-49 (S.D.N.Y. 2004) (precluding testimony discussing and evaluating drug company's conduct against FDA standards where witnesses lacked expertise regarding the FDA regulatory process); *In re: Diet Drugs*

Products Liab. Litig., No. MDL 1203, 2001 U.S. Dist. LEXIS 1174 at *27-28, 61-63 (E.D. Pa. Feb. 1, 2001) (excluding proposed testimony regarding content of drug label and compliance with regulations by physician who had "little or no knowledge" of regulations governing pharmaceutical company conduct and other physicians who had only "incidental experience with FDA regulations addressing the approval process for labeling, the requisite content of labels, or any other issues concerning the propriety of labeling as defined by FDA regulations").

Dr. Saklad's lack of qualifications is further demonstrated by his misunderstanding of applicable FDA regulations. According to Dr. Saklad, the proposed language regarding reports of compulsive behaviors that GSK submitted to FDA in July 2005 was not incorporated into the Requip labeling until October 2006. *See* Saklad Report at 3; Saklad Depo. at 160:18-161:2. In fact, that language became part of the Requip labeling in July 2005 pursuant to the FDA's "Changes Being Effected" provisions, which do not require FDA's prior approval of a manufacturer's labeling changes, *see* Rogers Depo. at 171:10-176:2 (Exhibit V) – something Dr. Saklad admitted he did not know. Saklad Depo. at 215:5-12. Dr. Saklad is plainly unqualified, and his testimony on the labeling issues should be precluded.

B. Dr. Wells Cannot Recover Absent Expert Testimony To Support His Failure To Warn Claim

In complex cases such as this one, legally-sufficient testimony from a qualified expert witness is necessary to establish whether a defendant's product warnings are adequate. *See* TEX. R. EVID. 702; *Goodyear Tire & Rubber Co. v. Rios*, 143 S.W.3d 107, 117-18 (Tex. App.—San Antonio 2004) ("Given the limited amount of space on a tire's sidewall and the many warnings and instructions pertinent to the operation, mounting, maintenance, and repair of a tire, we conclude that expert testimony was required . . . ."). As numerous courts have recognized, this principle is especially relevant in cases like the present one, involving a drug manufacturer's

alleged failure to warn. *See Bogle v. Sofarmor Danek Group, Inc.*, No. 95-864CIVRYSKAMP, 1999 WL 1132313, at *4 (S.D. Fla., Apr. 9, 1999) ("In the case of a drug manufacturer's duty to warn of a drug's dangerous side effects . . . [e]xpert testimony must . . . be used to establish the inadequacy of the warning"); *Haggerty v. Upjohn Co.*, 950 F. Supp. 1160, 1168 (S.D. Fla. 1996) "[B]ecause a manufacturer's duty to warn of a drug's hazards runs to the physician, the adequacy or inadequacy of a manufacturer's warning to inform a physician must also be proved by expert testimony"), *aff'd*, 158 F.3d 588 (11th Cir. 1998); *accord, Webster v. Pacesetter, Inc.*, 259 F. Supp. 2d 27, 36 n. 10 (D.D.C. 2003); *Langer v. Dista Prods. Co.*, No. 90 C 4598, 1996 WL 526763, at *2 (N.D. Ill. Sept. 12, 1996); *Northern Trust Co. v. Upjohn Co.*, 213 Ill. App. 3d 390, 398-99, 572 N.E.2d 1030, 1035-37 (Ill. App. 1991); *Docken v. CIBA-GEIGY*, 101 Or. App. 252, 256, 790 P.2d 45, 47 (Or. App. 1990); *Dion v. Graduate Hospital of Univ. of Pa.*, 360 Pa. Super. 416, 426, 520 A.2d 876, 881 (Pa. Super. Ct. 1987).

Because Dr. Saklad's proposed testimony as to the adequacy of the Requip labeling is not admissible, and Dr. Wells has proffered no other expert testimony to support his failure to warn claim, Dr. Wells cannot recover; and this is an additional ground on which GSK is entitled to summary judgment.

CONCLUSION AND PRAYER

For the reasons stated above, GSK's motion to preclude the testimony of Dr. Wells' proposed expert witnesses should be granted, and GSK should be granted summary judgment dismissing Dr. Wells' first amended complaint.

Dated: July 21, 2008

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on the 21st day of July, 2008, I electronically filed the foregoing with the Clerk of Court using the CM/ECF system, which will send notification of such filing to the following:

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